

WORKING GROUP :           Biologicals Quality Monitoring.

TOPIC:                       *Test on the absence of extraneous agents*

## ***REVISED   FORMAT***

### **DRAFT TEXT**

#### **GUIDELINE FOR THE TESTS TO DETERMINE THE PRESENCE OF EXTRANEIOUS AGENTS IN VETERINARY VACCINES.**

##### **A. Mammalian viral vaccines produced in established cell-lines.**

*Part II. Tests to determine the presence of extraneous agents other than viruses.*

**Date :   VS 2000/01**

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## **1.INTRODUCTION.**

### **1.1 Objective of the guideline.**

It is important that biological products for veterinary use are free of contaminants. Potential sources of contamination are the viral and bacterial strains used for the production of the active ingredient(s) and the starting materials of animal origin used in the production of the active ingredient and / or in the assembly of the finished product. Consequently it is necessary to demonstrate that extraneous agents are not present in biological products nor in the starting materials required for their manufacture, through the use of accepted testing procedures and sampling methods and subject to the limitations of the test.

The purpose of the guideline is to provide a description of the test methods to detect the presence of extraneous agents other than viruses which shall be undertaken on all materials of animal origin used in the production of veterinary immunological products for use in mammals. It shall also provide precise information on the method and conditions of the tests to determine the absence of extraneous viruses in these substances.

### **1.2. Background.**

The materials used in the manufacture of biological products for veterinary use can be divided into two main categories:

1. Viral strains and cell substrates used in the production of the active ingredient(s).
2. Starting materials of animal origin used in the production of the active ingredients and/or in the assembly of the finished product.

Restrictions may be placed by regulatory authorities upon the use of starting materials of animal origin to minimise the risk associated with pathogens that may be potentially present in these materials e.g.: their use is not generally acceptable except when they are sterilised by a suitable, validated method.

Where the use of such substances has been shown to be essential and sterilisation not possible, it will normally be required to test and monitor the source animals for freedom from infectious agents and/or to test these substances for the absence of contaminants. [ *In the case of inactivated vaccines, the method used for inactivation of the vaccine strain may also be validated for inactivation of possible contaminants from substances of animal origin.* ]

Present methods of testing for extraneous agents of substances of animal origin are described in the European Pharmacopoeia monograph 62 (1995) and in the Code of Federal Regulations 9CFR 113 and the OIE Manual of Standards for Diagnostic Tests and Vaccines.

[ *The use of experimental animals in tests shall be minimised and if required its necessity shall be justified* ]

### 1.3. Scope of the guideline.

The scope of the guideline is to provide guidance on the methods to determine the presence of extraneous agents other than viruses in veterinary viral vaccines for mammals manufactured in established cell lines.

The test methods are intended for the test on starting materials of animal origin used in the manufacture of the vaccine e.g. seeds and cell stocks and on the finished and intermediate products.

In principle its scope is limited to those agents which will not be detected with the normal sterility test method. This test method has already been agreed upon by the Japanese Pharmacopoeia, USP and Eur.Ph.

*Remark: Mycoplasma spp. can be excluded as well because they can be detected with the method presently under harmonisation within the VICH process.*

## 2. GUIDELINE FOR TESTING FOR PRESENCE OF EXTRANEEOUS AGENTS OTHER THAN VIRUSES IN MAMMALIAN VIRAL VACCINES.

### 2.1. Test for the presence of ( agent A )

#### 2.1.1. General.

#### 2.1.2. Samples

#### 2.1.3. Substrates

#### 2.1.4. Test method

*Remark: Under these sections the test methods for the different agents have to be fully described or references made to test methods described in a Pharmacopoeia .*

### NOTE:

In the list of Extraneous agents published by the European Commission ( document III/3472/93) the following non-viral agents are listed:

### BOVINES , CAPRINES AND OVINES:

- Brucella abortus
- Brucella ovis
- Brucella melitensis
- Leptospira spp.
- Mycobacterium tuberculosis,
- Mycobacterium paratuberculosis
- Mycoplasma spp.
- Coxiella burnetti

- Chlamydia ovis
- Salmonella spp.

#### **PORCINES:**

- Actinobacillus pleuropneumonia
- Bordetella bronchiseptica
- Brucella suis
- Erysipelothrix rhusiopathiae
- Leptospira spp.
- Mycoplasma hyopneumoniae
- Mycoplasma hyorhinus
- Pasteurella multocida

#### **EQUINES:**

- Mycobacterium pseudomallei
- Streptococcus equi
- Trypanosoma spp.

#### **FELINES.**

None.

#### **CANINES.**

- Brucella canis
- Leptospira

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EXTRANEOUS AGENTS OTHER THAN VIRUSES.

*Please indicate your opinion whether or not sterility test is acceptable. If not please give reference to the test that shall be used and return the table .*

Agent	Sterility test Acceptable  ( Yes/No)	Reference or description of test required or normally done in			VICH proposal
		Japan	USA	EU	
<b>BOVINES , CAPRINES AND OVINES</b>					
Brucella abortus					
Brucella ovis					
Brucella melitensis					
Leptospira spp.					
Mycobacterium tuberculosis,					
Mycobacterium paratuberculosis					
Mycoplasma spp.					
Coxiella burnetti					
Chlamydia ovis					
Salmonella spp.					
<b>PORCINES:</b>					
Actinobacillus pleuropneumonia					
Bordetella bronchiseptica					
Brucella suis					
Erysipelothrix rhusiopathiae					
Leptospira spp.					
Mycoplasma hyopneumoniae					
Mycoplasma hyorhinus					
Pasteurella multocida					
<b>EQUINES</b>					

Streptococcus equi					
Trypanosoma spp.					
Mycobacterium pseudomallei					
<b>CANINES.</b>					
Brucella canis					
Leptospira spp.					